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Suspected Brucellosis Case Prompts Investigation of Possible Bioterrorism-Related Activity --- New Hampshire and Massachusetts, 1999

Brucella species, particularly *B. melitensis* and *B. suis*, are potential agents of biological terrorism (1,2). This report describes the public health and law enforcement assessment of a suspected case of brucellosis in a woman, in which the atypical clinical presentation and suspicious circumstances surrounding the case raised the possibility of biological terrorism. Although the investigation did not identify evidence of biological terrorism, the safe resolution of the case illustrates the value of integrated clinical, public health, and law enforcement biological terrorism preparedness and response.

On March 25, 1999, a 38-year-old woman who resided in New Hampshire was admitted to hospital A in New Hampshire with fever, myalgia, and weakness, which progressed over 3 days to respiratory failure requiring mechanical ventilation. On day 22, after 3 weeks of intensive care, the patient was transferred to hospital B in Boston, Massachusetts. Paired serum specimens obtained on day 4 and day 22 showed a 16-fold rise in titer (from 1:20 to 1:320) for *Brucella* antibodies by slide agglutination testing at hospital B. Cultures of blood were negative for *Brucella* species.

Hospital personnel interviewed family members who reported no history of traditional risk factors for *Brucella* exposure (e.g., relevant food, infected animal contact, or travel history). Although the rapid respiratory decompensation was not typical for brucellosis infection, the serologic findings met the surveillance case definition for brucellosis (3). As a result, hospital B made a routine case report of brucellosis to the Boston Public Health Commission (BPHC) on day 23.

On day 24, the patient's family reported to hospital personnel that the patient's illness might have been caused by exposure to "laboratory flasks" and "cultures" kept in her apartment by her boyfriend. He was described as a foreign national studying marine biology who was formerly affiliated with a local university but recently had returned to his country of citizenship. On day 25, the patient's family brought laboratory flasks, petri dishes, and culture media to hospital B from the patient's apartment. Several contained an unidentified clear liquid, and some were marked with dates from the 1980s. Infection-

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control staff at hospital B were notified of the laboratory-like materials on day 27. The positive *Brucella* antibody serology in association with the unusual laboratory-like equipment in the patient's residence and the acknowledged potential for *Brucella* species to be used as a bioterrorist agents raised concerns among the infection-control staff that this case might be associated with a bioterrorist event or unintentional exposure to contaminated materials in the patient's home. Hospital B contacted local law enforcement in New Hampshire and BPHC. After discussion with BPHC, the hospital B laboratory retested the patient's paired serum specimens for both *Brucella* and *Francisella tularensis* antibodies. The specimens tested negative for tularemia but remained positive for *Brucella* antibodies. BPHC then notified the Massachusetts Department of Public Health (MDPH) and the Federal Bureau of Investigation about the unusual circumstances surrounding the case.

On day 28, CDC and the New Hampshire Department of Health and Human Services (NHDHHS) were notified. NHDHHS had received no reports of brucellosis through its passive surveillance system. In response to the case report, NHDHHS contacted hospital infection-control nurses, but identified no other cases of unusual febrile illness or brucellosis in southern New Hampshire during the preceding few weeks. In Massachusetts, public health authorities identified two additional cases of brucellosis during the previous 3 months, compared with an average state incidence of one to two cases per year. However, review of the cases revealed that both persons had consumed unpasteurized goat's milk or cheese during international travel.

On day 30, under the authority of state communicable disease statutes and in cooperation with the local police department, fire department, and hazardous materials unit, NHDHHS personnel entered the New Hampshire patient's apartment to assess any possibility of an ongoing public health hazard. No laboratory materials or biological hazards were found. Further epidemiologic investigation by federal and state public health authorities identified no common exposures among the three cases. The laboratory materials originally brought to hospital B by the family were cultured at MDPH and then sent to the Armed Forces Institute of Pathology for further testing, where they tested negative when screened for several potential bioterrorism agents, including *Brucella* species.

On day 33, tube agglutination testing on the patient's paired serum specimens from day 4 and day 22 was negative for *Brucella* antibodies at CDC. On the same day at hospital B, the patient died from adult respiratory distress syndrome. An autopsy was requested by public health authorities; however, the possibility of a biological terrorist threat created concern on the part of the hospital pathology staff and the autopsy was postponed. Further testing of the patient's tissue samples was conducted through the CDC Unexplained Deaths and Critical Illness Surveillance Project, including immunohistochemistry for *Brucella*; although no diagnosis has been confirmed, CDC testing results and the patient's prolonged antecedent medical history of multiple febrile illnesses over the past decade suggest an unspecified autoimmune process.

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Editorial Note:

In this report, an initial serologic diagnosis of brucellosis was complicated by an unusual clinical presentation and other circumstances raising suspicion of a criminal act or possible biological terrorism (2--4). Although this case did not represent an actual biological crime or terrorism event, and brucellosis was ruled out as a cause of the patient's illness, this report highlights several key aspects of effective public health response to a possible biological terrorism crime or terrorism threat involving a biological agent or other unusual or unexplained illness. These aspects include 1) sensitive, specific, and rapid laboratory diagnosis of patients and characterization of biological agents; 2) early detection through improved surveillance; 3) effective communication; and 4) coordinated local, state, and federal response in the investigation of unusual events or unexplained illnesses.

Early detection is essential to ensure a prompt response to a biological terrorist event. Local public health authorities must rely on clinicians to recognize and report suspicious or unusual presentations of disease. However, correlating suspicious cases originating from diverse locations or discerning an increase in common presentations above the normal baseline is difficult. As in this case, public health practitioners coordinating disease surveillance may be able to receive reports of rare diseases and to determine whether they are occurring at a higher than normal rate in a large surveillance area.

CDC, in collaboration with local, state, and territorial health departments, is enhancing existing disease surveillance systems for specific diseases that are normally rare in the United States but thought to have a high potential for public health impact if used as biological terrorism agents (5,6). This is being accomplished by improving training of clinical, laboratory, and public health personnel in recognizing suspicious disease presentations and by expanding of existing, disease-specific surveillance infrastructure. In addition, surveillance is being improved for disease presentations such as acute respiratory distress, hemorrhagic, or meningeal symptoms normally caused by common infectious agents but that could indicate an increase in illnesses caused by a biological agent used in terrorism. Surveillance mechanisms to rapidly assess changes in rates of disease include monitoring of calls to local emergency medical systems, regularly reviewing emergency department discharge diagnoses, and linking infection control practitioner networks.

This report illustrates the dilemmas inherent in laboratory detection of potential agents of biological terrorism. Although the standard laboratory test for *Brucella* antibody is the tube agglutination test (7), the more rapid simple slide agglutination test is commonly used in commercial and hospital laboratories. The slide agglutination test is 97%--100% sensitive and may be as low as 88% specific (8). However, if used in a population with a low prevalence of disease, even a diagnostic test with 99% specificity will have a low positive predictive value. Because agents high on the list of possible biological terrorism have very low incidence of natural infection in the United States, the risk for a false-positive result is high. Therefore, diagnostic laboratory testing should be integrated with epidemiologic investigation when assessing potential covert biological terrorism events to rule out false-positive laboratory findings. To ensure that evaluation of materials from suspected biological terrorism events or threats is sensitive, specific, and rapid, CDC is working with its public health partners to improve laboratory diagnostic tests for many of the potential agents of biological terrorism and to transfer these diagnostic capabilities to state health department laboratories (6). CDC and other federal, state, and territorial public health laboratories are creating a multilevel Laboratory Response Network for Biological Terrorism that links state and local public health agencies to advanced capacity facilities that collectively maintain state-of-the-art capabilities for a wide range of biological agents.

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